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EXAMINER	
WOLLENBERGER, LOUIS V	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,487	MCSWIGGEN, JAMES	
	Examiner	Art Unit	
	Louis V. Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,10-21,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,10-21,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/31/06; 10/3/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

CRF Sequence Listing

Applicant's submission of a substitute CRF copy of the sequence listing in the reply filed on 3/27/07 is acknowledged. The CRF has been found to be error-free and has been entered into the application. The application is now in compliance with the Sequence Rules.

Status of Application/Amendment/Claims

Applicant's response filed 12/8/2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 8/8/2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 12/8/2005, claims 1, 3, 10–21, 30, and 31 are pending and currently under examination.

Oath/Declaration

Applicant's submission of a new Oath/Declaration in the reply filed 12/8/2005 is acknowledged. The submission corrects the defects noted in the previous Action.

Claim Objections/Notice of non-compliant amendment

The previous Action objected to Claim 1 because Step b was missing the word "a" before "nucleotide sequence". Applicants indicate in their Remarks, page 7, that the claim has been amended to insert the word "a." However, while the claim now contains the article "a" before "nucleotide", the "a" has not been underlined to indicate the changes that have been made relative to the immediate prior version of the claims, as required by 37 CFR §1.121(c)(2). In the interest of compact prosecution, the claims will be examined without further interruption. However, Applicant is requested to correct the deficiency in replying to this Action.

Information Disclosure Statement

The information disclosure statement (IDS) filed 10/3/05 fails to comply with the provisions of 37 CFR 1.98(b)(5).

The IDS has been placed in the application file, but the information referred to therein as GenBank Accession Nos. at pages 20-23 of the IDS have not been considered because the publication date of the documents have not been provided (37 CFR 1.98(b)(5)).

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Rejections - 35 USC § 112, second paragraph—new

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 10–21, 30, and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As amended on 12/8/2005, independent claim 1 now requires that the antisense strand of the claimed double stranded nucleic acid be complementary to "a human huntingtin (ICAM) nucleotide sequence comprising SEQ ID NO:439."

Neither the specification nor the prior art discloses any evidence that would show that, at the time of filing, one of skill in the art would recognize or appreciate the correlation, homology, or identity between ICAM sequence SEQ ID NO:439 and the huntingtin gene, nor any discussion of the direct association of ICAM sequence SEQ ID NO:439 with Huntington's disease.

Applicant states in the Remarks, page 6, that SEQ ID NO:439 corresponds to GenBank entry NM_000201; however, a review of this sequence in PubMed finds that the sequence corresponds to human intercellular adhesion molecule 1, or ICAM1, and there is no further disclosure thereof clearly linking ICAM1 with any huntingtin gene. The scope and meaning of the limitation "a human huntingtin (ICAM) nucleotide sequence comprising SEQ ID NO:439" is therefore unclear, rendering the metes and bounds of the claims as a whole unclear.

Correction and/or clarification is required.

For purposes of this examination, the claim is interpreted as being drawn to double stranded nucleic acids complementary to an ICAM sequence comprising SEQ ID NO:439.

Claim Rejections - 35 USC § 112, first paragraph—withdrawn

The rejection of Claims 1-31 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicant's amendment to the claims.

Claim Rejections - 35 USC § 112, first paragraph—new

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 10–21, 30, and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendment to the claims submitted on 12/8/05 introduces the limitation "a human huntingtin (ICAM) nucleotide sequence comprising SEQ ID NO:439" into independent claim 1.

MPEP 2163, Section II, Part A, states in part that there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed, *Wertheim*, 541 F.2d at 262, 191 USPQ at 96; however, with respect to newly added or amended claims, applicant should show support in the original disclosure for the new or amended claims.

To comply with the written description requirement of 35 U.S.C. 112, para. 1, or to be entitled to an earlier priority date or filing date under 35 U.S.C. 119, 120, or 365(c), each claim

limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure. When an explicit limitation in a claim "is not present in the written description whose benefit is sought it must be shown that a person of ordinary skill would have understood, at the time the patent application was filed, that the description requires that limitation." *Hyatt v. Boone*, 146 F.3d 1348, 1353, 47 USPQ2d 1128, 1131 (Fed. Cir. 1998). See also *In re Wright*, 866 F.2d 422, 425, 9 USPQ2d 1649, 1651 (Fed. Cir. 1989) (MPEP 2163).

In the instant case, while Applicant points to specific pages in the instant application as support for the claim amendments (see Remarks, page 6), explicit, implicit, or inherent support for the newly added limitations is not found in these citations or anywhere else in the specification as filed. Specifically, written description support does not exist for siRNAs or any other double stranded nucleic acid complementary to a human huntingtin ICAM sequence corresponding to SEQ ID NO:439. While support does exist for RNAs complementary to human intercellular adhesion molecule 1, or ICAM1, corresponding to SEQ ID NO:439, the association of this gene with the huntingtin gene is not disclosed in the instant application. In fact the term "huntingtin" is not found at all.

Accordingly, the instant claims as a whole are rejected for lack of written description support.

Dependent claims 3, 10–21, 30, and 31 are rejected therefor.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant points to support for the instant

claims in prior filed US Provisional Application 60/363,124, filed 3/11/2002 (see Remarks, pages 7-9).

While support is found for claims to chemically modified double stranded nucleic acids complementary to NM_000201 (see GenBank entry in Table III, page 383 and page 10 of the specification, for example), support does not exist in prior filed application 60/363,124 for the instantly amended claims for the reasons given above in the rejection under 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102—withdrawn

The rejections of Claims 1, 3-9, 14, 20, 23-28 and 31 under 35 U.S.C. 102(a) as being anticipated by Kretschmer-Kazemi Far et al. and of Claims 1-11, 14, 20, 21,23-29 and 31 under 35 USC 102(a) as being anticipated by Reich et al. are withdrawn in view of applicant's amendments to the claims.

Kretschmer-Kazemi Far et al. does not teach siRNAs directed specifically to SEQ ID NO:439 and comprising at least two different chemically modified nucleotides.

Claim Rejections - 35 USC § 103—withdrawn

To clarify, the previous Action mailed 8/8/05 inadvertently cited claims 36-69 as rejected under this section; however, the Action addressed the limitations present in pending claims 1, 3, 10–21, 30, and 31. To be clear, then:

The rejection of Claims 1, 3, 10–21, 30, and 31 under 35 U.S.C. 103(a) as being unpatentable over Elbashir et al., in view of Nyce et al. (WO 96/40162), Tuschl et al. (WO 02/44321), Matulic-Adamic et al. (U.S. 5,998,203), and Morrissey et al. (US 2003/0206887) is

withdrawn in view of Applicant's amendment to the claims. The cited references as a whole do not teach SEQ ID NO:439.

Applicant's arguments submitted 12/8/05 in response to the previous rejection under this section are addressed below as they pertain to the new rejection.

Claim Rejections - 35 USC § 103—new

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3, 10–21, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett et al. (US Patent 6111094); Agrawal et al. (WO 94/01550); Matulic-Adamic et al. (U.S. 5,998,203), and GenBank Accession No. NM_000201, published on the World Wide Web by NCBI on October 31, 2000 [retrieved on May 17, 2007].

With entry of the amendment filed on December 8, 2005, the claims are now drawn to a chemically synthesized double stranded nucleic acid molecule comprising a sense and antisense strand of about 18 to about 27 nucleotides in length, wherein the antisense strand is complementary to a human huntingtin (ICAM) sequence comprising SEQ ID NO:439.

Applicants states in the Remarks filed 12/8/05, page 6, that SEQ ID NO:439 represents GenBank entry NM_000201, and appeared in GenBank on Oct. 31, 2000.

A printout of the October 31, 2000 GenBank entry as published on that date is attached herewith, and has been incorporated into the instant rejection to address the new limitations. The NCBI on-line publication shows the mRNA sequence for human intercellular adhesion molecule

1, ICAM1, was known in the prior art. The publication contains a detailed bibliography of prior art references describing the physical and biochemical characteristics of the gene.

The amendment has also deleted references to cleavage of the ICAM RNA and removes the term "siNA" from the claims and requires the presence of at least two different chemical modifications. Thus, both broadening and narrowing amendments have been made to the claims.

The claims read on any chemically modified double stranded nucleic acid complementary to ICAM1, SEQ ID NO:439.

The claims do not require any specific function or activity; thus, the claims embrace a variety of double stranded molecules, including double stranded antisense molecules and self-stabilized ribozymes, as taught by Agrawal et al.

Applicant is further reminded that the instant specification teaches at page 12 (paragraph 28 in the application publication) that 2'-deoxyribonucleotides (i.e., DNA) are considered by Applicant to be chemically modified nucleotides within the scope of the instant application.

Bennett et al. taught antisense oligonucleotides targeted to human ICAM1. It is taught that Expression of ICAM-1 has been associated with a variety of inflammatory skin disorders, and that it is has been hoped that inhibitors of ICAM-1 would provide a novel therapeutic class of anti-inflammatory agents with activity towards a variety of inflammatory diseases or diseases with an inflammatory component such as asthma, rheumatoid arthritis (col. 2). It is taught that antisense compounds avoid many of the pitfalls of other agents that could potentially be used to block the effects of ICAM-1 (col. 2). It is taught that antisense oligonucleotides are commonly used as research reagents, diagnostic aids and therapeutic agents and that nucleic acids encoding

intercellular adhesion molecule-1 (ICAM-1; also known as CD54 antigen) proteins, including human ICAM-1, are particularly amenable to the antisense approach for therapeutic uses (col. 3). It is taught that the antisense compounds may comprise from about 8 to about 30 nucleobases, and may be chemically modified with one or more sugar, nucleobase, and/or internucleotide linkage modification at one or more positions within the sequence to enhance the stability and/or activity of the antisense oligonucleotide, including such modifications as recited in the instant claims such as 2'-O-methyl and 2'-fluoro modifications. (col. 6, and cols. 8-10). It is also taught that the chemically modified antisense oligonucleotides may comprise RNA or DNA nucleotides (col. 6). Several representative embodiments are described and exemplified (cols. 35 *et seq.*).

Bennett et al. do not teach double stranded antisense oligonucleotides targeted to SEQ ID NO:439, or oligos thereof that contain inverted abasic moieties.

Agrawal et al. taught self-stabilized, double-stranded, hairpin oligonucleotides comprising a target hybridizing region and a self complementary region that form a totally or partially double stranded structure that is resistant to nucleolytic degradation (pg. 5, lines 13-17, 25–30). The self-stabilized oligonucleotides are specifically designed for inhibiting gene expression in cells in vitro and in vivo by inducing RNase H-mediated cleavage of a target mRNA (pages 5-6).

The target hybridizing and a self complementary regions of the oligonucleotide can be composed of ribonucleotides, deoxyribonucleotides, or both, with ribonucleotide and/or deoxyribonucleotide monomers being connected together via 5' to 3' linkage (pages 8–16, for example). Additionally, it is taught that the oligonucleotide may include modified nucleic acid bases and/or sugars as well as molecules having added substituents, such as diamines,

cholesteryl, or other lipophilic groups (pg. 8). In one preferred embodiment, the self-stabilized oligonucleotide is rendered hyperstabilized by incorporating one or more 2'-O-Me ribonucleotides into the self-complementary region. The target hybridizing region may contain ribonucleotides or 2'-O-Me-ribonucleotides and the self-complementary region may contain DNA" (page 16).

Agrawal et al. disclose that the target hybridizing region is from about 8 to about 50 nucleotides in length (pgs. 9-10), that the self complementary region can span the target hybridizing region, that the complementary sequences form base pairs resulting in a hairpin structure and that the intramolecular base pairing can be so extensive as to involve every nucleotide of the oligonucleotide (pg. 15 and see Fig. 5). Fig. 5, cmpd C, for example, shows a fully complementary, expression-inhibiting hairpin oligonucleotide having a double stranded region spanning 17 bases. Agrawal et al. also taught self-stabilized ribozymes, comprising both sense and antisense strands (Fig. 7)

With regard to claims 10-12, Agrawal et al. taught that the target hybridizing region (i.e., antisense strand) and self complementary region (i.e., a sense strand) of a self-stabilized, hairpin oligonucleotide may be connected by a suitable "non-nucleic acid linker" (page 15, lines 30-36).

Agrawal et al. also teach that the target hybridizing region and self complementary regions may be composed of RNA, DNA, or both (see page 16, lines 5-10, for example).

Agrawal et al. further taught and suggested that 5' and 3' capping agents may be added to stabilize antisense oligos against exonuclease degradation (page 3 and 19, for example). For example, Agrawal et al. explicitly taught that "Even greater resistance to nuclease degradation

can be provided by using nuclease resistant internucleotide linkages near or cap structures at one or both ends of the oligonucleotide" (page 19).

Accordingly, Agrawal et al. taught and suggested methods for inhibiting gene expression in a cell using a self-complementary, chemically modified, RNA and/or DNA-containg, hairpin nucleic acid molecule, composed of two distinct strands joined via a non-nucleic acid linker.

Matulic-Adamic et al. (U.S. Patatent 5,998,203) taught double stranded nucleic acids comprising inverted abasic terminal cap moieties that provide resistance to degradation (see column 2, lines 44-55; column 3 lines 1-68; columns 8-9; and Fig. 13). Matulic-Adamic et al. further teach a double stranded structure comprising separate sense and antisense strands and further wherein this structure comprises a connecting loop comprising a linker or non-nucleotide linker (see Figure 3). Matulic-Adamic et al. taught the incorporation of chemical modifications at the 5' and/or 3' ends of the nucleic acids to protect the enzymatic nucleic acids from exonuclease degradation, which improves the overall effectiveness of the nucleic acid, as well as facilitates uptake of the nucleic acid molecules (see column 2). Matulic-Adamic et al. teach base, sugar and/or phosphate modification, as well as terminal cap moieties at the 5'-cap, 3'-cap, or both. Specifically, 3' phosphorothioates, inverted abasic moieties, and 2'-O-methyl modifications are utilized. Matulic-Adamic et al. teach 2'deoxy nucleotides and 2'-deoxy-2'-halogen nucleotides, wherein Br, CL and F are representative halogens (see column 3, for example).

One of skill in the art of antisense and ribozyme technologies would appreciate that the use of inverted abasic moieties for the protection against nuclease degradation in ribozymes could be readily transferred for use in antisense oligonucleotides for the same purpose using routine methods to further protect self-stabilized antisense oligonucleotides against exonuclease

degradation, as suggested by Agrawal et al. (pages 3 and 19), in the same way that such terminal modifications provide for exonuclease resistance in ribozymes as explicitly taught by Matulic-Adamic et al. (see, for example, cols. 2 and 3).

Accordingly, it would have been obvious at the time the instant invention was made to make and use chemically modified, double stranded, self-stabilized, hairpin antisense oligonucleotides of the type taught by Agrawal et al. to inhibit the expression of human ICAM1 for the reasons taught by Bennett et al. It would further have been obvious and a matter of routine experimentation to incorporate one or more chemical modifications into the self-stabilized antisense oligonucleotide to further stabilize the oligonucleotide against nuclease degradation, as taught by Agrawal et al. (page 16, for example), Bennett et al., and Matulic-Adamic et al. using the materials and methods taught by Agrawal et al., Bennett et al., and Matulic-Adamic et al. In view of Bennet et al., it would have been obvious to one of skill at the time of invention that any human ICAM1 gene known in the art would be of both research and therapeutic interest. Human ICAM1 sequence SEQ ID NO:439 was known in the prior art, as evidenced by Applicant's remarks filed 12/8/05, page 6, and by the online publication of the sequence and bibliography available from NCBI (GenBank).

For these same reasons one of skill would have been well motivated and have had a reasonable expectation of success given that the combination of cited prior art references as a whole teach and/or suggest making and using chemically modified antisense oligonucleotides targeted to human ICAM1 for investing ICAM1 function and as possible therapeutics to treat disease associated with ICAM1 expression. One of skill would have been motivated to make and use double stranded antisense oligonucleotides with chemical modifications given that Agrawal

et al. together with Bennet et al. and Matulic-Adamic et al. expressly taught that such molecules are superior to conventional antisense molecules with regard to their stability and duration of activity, that such molecules may consist of RNA, DNA, or both RNA and DNA, and that such molecules may be further modified at the both terminal and internal residues at the 2'-sugar and internucleoside phosphate moieties with 2'-O-methyl and 2'-fluoro and inverted abasic moieties to further enhance stabilities and acitivities.

Thus, the references taught and suggested double stranded nucleic acid molecules complementary to ICAM1 sequence SEQ ID NO:439 having at least two different chemical modifications. Applicant will note that the instant specification teaches at page 12 (paragraph 28 in the application publication) that 2'-deoxyribonucleotides are considered by Applicant to be a "chemical modification" within the scope of the instant application. Agrawal et al. clearly taught that self-stabilized antisense oligonucleotides may comprise DNA as well as RNA, and that such constructs may further contain phosphorothioate and/or 2'-O-methyl modifications.

Accordingly, in the absent of convincing evidence to the contrary, the instantly claimed invention would have been *prima facie* obvious to one of skill in the art at the time the invention was made.

Response to Arguments

In response to the previous rejection, Applicant argues the rejection as applied to claims drawn to RNAi-active molecules (page 12). However, as amended on 12/8/05, the claims no longer require RNAi activity, nor any function at all. Thus, features upon which applicant relies (i.e., RNAi) are not recited in the rejected claim(s). Although the claims are interpreted in light

of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The claims have been broadened to include any double stranded nucleic acid having at least two chemical modifications targeted to ICAM1 SEQ ID NO:439. Although the claims continue to embrace siRNA, they are not limited to siRNA nor do the claims require RNAi activity or any other particular activity.

Applicant has argued that Matulic-Adamic et al. taught modifications of ribozymes, that ribozymes, antisense, and siRNAs are non-analogous, and that Matulic-Adamic et al. is not pertinent to the problem addressed by the instantly claimed compounds. Applicant appears to argue there is not motivation for one of skill in either the RNAi or antisense arts to look to the problems faced by and solutions taught by those in the ribozyme and/or antisense arts.

The Examiner respectfully disagrees. The Examiner refers to MPEP 2141.01, which states in part that " The examiner must determine what is "analogous prior art" for the purpose of analyzing the obviousness of the subject matter at issue. "In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant"s endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). See also *In re Deminski*, 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986); *In re Clay*, 966 F.2d 656, 659, 23 USPQ2d 1058, 1060-61 (Fed. Cir. 1992) ("A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem."); *Wang Laboratories Inc. v. Toshiba Corp.*,

993 F.2d 858, 26 USPQ2d 1767 (Fed. Cir. 1993); and *State Contracting & Eng'g Corp. v. Condotte America, Inc.*, 346 F.3d 1057, 1069, 68 USPQ2d 1481, 1490 (Fed. Cir. 2003) (where the general scope of a reference is outside the pertinent field of endeavor, the reference may be considered analogous art if subject matter disclosed therein is relevant to the particular problem with which the inventor is involved)."

Problems faced by those in the ribozyme and/or antisense fields are reasonably pertinent to problems faced by those in the siRNA and/or antisense fields.

The instant case is analogous to that presented in Section III of MPEP 2141.01, which states "The court found that because PTFE and rubber are used by the same hose manufacturers and experience the same and similar problems, a solution found for a problem experienced with either PTFE or rubber hosing would be looked to when facing a problem with the other.); *In re Mlot-Fijalkowski*, 676 F.2d 666, 213 USPQ 713 (CCPA 1982) (Problem faced by appellant was enhancement and immobilization of dye penetrant indications. References which taught the use of dyes and finely divided developer materials to produce colored images preferably in, but not limited to, the duplicating paper art were properly relied upon because the court found that appellant's problem was one of dye chemistry, and a search for its solution would include the dye arts in general.)."

At the time of the instant invention, ribozymes, antisense, and siRNAs were recognized as members of a growing collection of oligonucleotide-based reagents for inhibiting gene expression in cells in vitro and in vivo. For example, Elbashir et al., page 496, directly compares and contrasts the activities and benefits of ribozymes, antisense, and siRNAs (see Elbashir et al., page 496, for example), showing that those of skill in the arts recognized the functional

equivalency of these reagents. Thus, ribozymes, antisense, and siRNAs have essentially the same function and essentially the same chemical features inasmuch as they each comprise chains of nucleotides and are all equally receptive to chemical modification at the sugar, phosphate, and nucleobase positions.

One of skill in the antisense or RNAi arts searching for a solution to the problem of oligonucleotide stability and activity would be commended to the solutions of others in the ribozyme and antisense arts who faced the same problem. Those of skill in the ribozyme and antisense arts solved the problem by incorporating chemical modifications into the sugar-phosphate backbone.

Recognizing that the same modifications could be incorporated into double stranded molecules, it would require nothing more than routine experimentation for one of skill in the antisense and/or RNAi art to select from the modifications shown in the prior art for enhancing ribozyme and antisense stability for incorporation into double stranded molecules of either the antisense and/or siRNA type. One of skill would have had a reasonable expectation of success in identifying a number of embodiments within the scope of the instantly claimed invention, given that Agrawal et al. showed and explicitly taught several such embodiments, and given that the instant claims explicitly embrace such hairpin-type oligonucleotides, as evidenced by claims 10-12. Furthermore, "Whether an art is predictable or whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made" (MPEP 2143.02).

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis V. Wollenberger whose telephone number is 571-272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Sean McGarry/
Primary Examiner AU 1635